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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/954,975	09/18/2001	Jack Stapleton	IOWA:033US/SLH	7706

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FULBRIGHT & JAWORSKI L.L.P.
SUITE 2400
600 CONGRESS AVENUE
AUSTIN, TX 78701

EXAMINER
CHOI, FRANK I

ART UNIT	PAPER NUMBER
1616	10

DATE MAILED: 04/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/954,975	Applicant(s) STAPLETON ET AL.	
	Examiner Frank I Choi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 11-40 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 11-40 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-13, 16-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murrer et al. (US Pat. 5,093,134) in view of the acknowledged prior art and Narashimhan et al. for the reason set forth in the prior Office Action and the further reasons below.

Murrer et al. teaches a composition containing gallium which is less toxic than AZT and HPA-23 which is effective against HIV-1 and HIV-2 (Columns 3,4, Table, Column 4, lines 60-64). It is taught that the active compounds may be administered by injection, or in a capsule or tablet (Column 5, lines 10-20). It is taught the compositions provide active compound in the dosage range in humans of from 0.1 to 100 mg/kg body weight per day, in a single dose or a number of smaller doses and that other active compounds may be used in the compositions or administered separately (Column 6, lines 3-14).

Applicant acknowledges that it is known that HIV results in rejection of T-lymphocytes because the same when infected with HIV are removed by host immune response and that the reduction of T-lymphocytes can lead to the development of AIDS (Pg. 2, lines 15-24). It is known that current treatments include treatment with dideoxynucleotides, such as AZT, dideoxyinosine and dideoxycytidine (Pg. 2, lines 27-29). It is known that inhibition of ribonucleotide reductase inhibits HIV replication and that ribonucleotide reductase inhibitors

potentiate the activity of dideoxynucleotides which are nucleoside reverse transcriptase inhibitors (Pg. 3, lines 8-20).

Narashimhan et al. teach that gallium inhibits ribonucleotide reductase (Abstract).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose a method of treating HIV in a human infected with the same with gallium and a composition or kit containing gallium and nucleoside inhibitor. However, the prior art amply suggests the same as it is known that compositions containing gallium are effective against HIV and are less toxic than AZT, that gallium is a ribonucleotide reductase inhibitor and that said ribnucleotide reductase inhibitors potentiate the effects of dideoxynucleotides. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that gallium containing compositions would be effective against HIV in humans and that the combination of gallium compositions with nucleoside inhibitors would result in more effective HIV therapy.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 231 USPQ 375 (Fed. Cir. 1986). Further, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 208 USPQ 871 (CCPA 1981). Further, the

acknowledged prior in combination with the cited prior art as indicated above amply suggests and would motivate one of ordinary skill in the use gallium as gallium inhibits ribonucleotide reductase which inhibitors are known to be effective in treating HIV.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 11-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over the acknowledged prior art in view of Narashimhan et al., Collery et al. (US Pat. 5,525,598) and Bernstein (US Pat. 5,883,088).

Applicant acknowledges that it is known that HIV results in rejection of T-lymphocytes because the same when infected with HIV are removed by host immune response and that the reduction of T-lymphocytes can lead to the development of AIDS (Pg. 2, lines 15-24). It is known that current treatments include treatment with dideoxynucleotides, such as AZT, dideoxyinosine and dideoxycytidine (Pg. 2, lines 27-29). It is known that inhibition of ribonucleotide reductase inhibits HIV replication and that ribonucleotide reductase inhibitors potentiate the activity of dideoxynucleotides which are nucleoside reverse transcriptase inhibitors (Pg. 3, lines 8-20).

Narashimhan et al. teach that gallium, for example gallium nitrate and gallium citrate, inhibit ribonucleotide reductase (Abstract).

Collery et al. teach that gallium complexes are effective in treating HIV and that gallium nitrate inhibits reverse transcriptase found in retroviruses, such as HIV (Column 1, lines 24-32, Columns 15,16, Table VII).

Bernstein teaches that gallium complexes of hydroxypyrones exhibit increased oral availability and are also suitable for administration intravenously (See entire document).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose a method of treating HIV in a human infected with the same with gallium and a composition or kit containing gallium and nucleoside inhibitor. However, the prior art amply suggests the same as it is known that compositions containing gallium are effective against HIV and are less toxic than AZT, that gallium is a ribonucleotide reductase inhibitor and that said ribnucleotide reductase inhibitors potentiate the effects of dideoxynucleotides. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that gallium containing compositions would be effective against HIV in humans and that the combination of gallium compositions with nucleoside inhibitors would result in more effective HIV therapy.

Examiner has duly considered Applicant's arguments but deems them unpersuasive for the same reasons as above.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machines are (703) 308-4556 or (703) 305-3592.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (703) 308-0067. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. José Dees, can be reached on (703) 308-4628. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (703) 308-1235 and (703) 308-0198, respectively.

FIC
April 21, 2003

JOHN PAK
PRIMARY EXAMINER
GROUP 1600